Diagnostic accuracy of mpMRI and fusion-guided targeted biopsy evaluated by transperineal template saturation prostate biopsy for the detection and characterization of prostate cancer

Mortezavi, Ashkan ; Märzendorfer, Olivia ; Donati, Olivio F ; Rizzi, Gianluca ; Rupp, Niels J ; Wettstein, Marian S ; Gross, Oliver ; Sulser, Tullio ; Hermanns, Thomas ; Eberli, Daniel

Abstract: PURPOSE To evaluate the diagnostic accuracy of mpMRI and mpMRI / transrectal ultrasound (TRUS) fusion-guided targeted biopsy (FTB) against transperineal template saturation prostate biopsy (TTSPB) for the detection of prostate cancer (PCa). PATIENTS AND METHODS Retrospective analysis of 415 men consecutively presenting for prostate biopsy between 11/2014 and 9/2016 at our tertiary care centre. MpMRI (3-Tesla, without endorectal coil) was performed followed by TTSPB with the BiopSee® fusion system. Additional FTB was carried out in men with a suspicious lesion on mpMRI (Likert score 3-5). Any Gleason pattern 4 was defined as clinically significant PCa (csPCa). Detection rates of mpMRI and FTB were compared with the detection rate of TTSPB using the McNemar test. RESULTS The median numbers of TTSPB and FTB cores taken were 40 (range 30-55) and three (2-4), respectively. Among 124 patients (29.9%) without suspicious lesion on mpMRI, 32 (25.8%) were found to have csPCa on TTSPB. Among 291 patients (70.1%) with a Likert score 3-5 on mpMRI, FTB detected 129 (44.3%), TTSPB 176 (60.5%) and the combined approach 187 patients (64.3%) with a csPCa. Overall, 58 cases (19.9%) of csPCa would have been missed if FTB was performed exclusively. Sensitivities of mpMRI and FTB for csPCa were 84.6% and 56.7%, with a negative likelihood ratio of 0.35 and 0.46, respectively. CONCLUSIONS MpMRI alone should not be used as a triage test due to a substantial number of false-negative cases with csPCa. Systematic biopsy outperformed FTB and will therefore remain crucial in the diagnostic pathway of PCa.

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Diagnostic Accuracy of Multiparametric Magnetic Resonance Imaging and Fusion Guided Targeted Biopsy Evaluated by Transperineal Template Saturation Prostate Biopsy for the Detection and Characterization of Prostate Cancer

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Purpose: We evaluated the diagnostic accuracy of multiparametric magnetic resonance imaging and multiparametric magnetic resonance imaging/transrectal ultrasound fusion guided targeted biopsy against that of transperineal template saturation prostate biopsy to detect prostate cancer.

Materials and Methods: We retrospectively analyzed the records of 415 men who consecutively presented for prostate biopsy between November 2014 and September 2016 at our tertiary care center. Multiparametric magnetic resonance imaging was performed using a 3 Tesla device without an endorectal coil, followed by transperineal template saturation prostate biopsy with the BiopSee® fusion system. Additional fusion guided targeted biopsy was done in men with a suspicious lesion on multiparametric magnetic resonance imaging, defined as Likert score 3 to 5. Any Gleason pattern 4 was defined as clinically significant prostate cancer. The detection rates of multiparametric magnetic resonance imaging and fusion guided targeted biopsy were compared with the detection rate of transperineal template saturation prostate biopsy using the McNemar test.

Results: We obtained a median of 40 (range 30 to 55) and 3 (range 2 to 4) transperineal template saturation prostate biopsy and fusion guided targeted biopsy cores, respectively. Of the 124 patients (29.9%) without a suspicious lesion on multiparametric magnetic resonance imaging 32 (25.8%) were found to have clinically significant prostate cancer on transperineal template saturation prostate biopsy. Of the 291 patients (70.1%) with a Likert score of 3 to 5 clinically significant prostate cancer was detected in 129 (44.3%) by multiparametric magnetic resonance imaging fusion guided targeted biopsy, in 176 (60.5%) by transperineal template saturation prostate biopsy and in 187 (64.3%) by the combined approach. Overall 58 cases (19.9%) of clinically significant prostate cancer would have been missed if fusion guided targeted biopsy had been performed exclusively. The sensitivity of multiparametric magnetic resonance imaging and fusion guided targeted biopsy for clinically significant prostate cancer was 84.6% and 56.7% with a negative likelihood ratio of 0.35 and 0.46, respectively.

Conclusions: Multiparametric magnetic resonance imaging alone should not be performed as a triage test due to a substantial number of false-negative cases with clinically significant prostate cancer. Systematic biopsy outperformed fusion guided targeted biopsy. Therefore, it will remain crucial in the diagnostic pathway of prostate cancer.

Abbreviations and Acronyms

csPCa = clinically significant PCa
FTB = fusion guided targeted biopsy
GS = Gleason score
LR = likelihood ratio
MCCL = maximum cancer core length
mpMRI = multiparametric MRI
MRI = magnetic resonance imaging
PCa = prostate cancer
ROI = region of interest
SB = systematic biopsy
TRUS = transrectal ultrasound
TTSPB = transperineal template saturation prostate biopsy

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THE introduction of mpMRI has allowed for noninvasive localization of areas suspicious for PCa, in contrast to traditional random sampling of the organ by TRUS guided biopsy.[1] Further technological advances led to a combination of those methods by introducing mpMRI/TRUS FTB platforms for targeted sampling of suspicious regions identified on imaging.[2,3]

To date the reference tests in studies evaluating the detection rate of FTB have been were standard TRUS guided biopsy[3] or whole gland histology.[4] However, each of these methods have inherent disadvantages for histopathological correlation. Standard TRUS guided biopsy is inaccurate.[5,6] Also, whole gland specimens introduce selection bias by only including patients diagnosed with PCa who qualify for radical treatment, thus, excluding men with false-negative biopsy results and low risk disease.[7,8]

It has been shown that FTB detects a higher proportion of csPCa with fewer cores than standard TRUS guided biopsies.[3] These results opened a debate on whether FTB alone without SBs might be sufficient to detect csPCa.[9,10]

In our study we compared the performance of mpMRI and mpMRI/TRUS fusion guided targeted biopsy with TTSPB, a reference standard with better representation of the disease in the prostate gland than standard TRUS guided biopsy.[11]

PATIENTS AND METHODS

Study Design and Patient Selection

This retrospective analysis included all men who underwent mpMRI followed by TTSPB with the BiopSee® fusion system between November 2014 and September 2016 at our academic tertiary care center. Patients previously treated for PCa were not included in study. Criteria described by the START (Standards of Reporting for MRI-Targeted Biopsy Studies) Consortium were followed when reporting this study.[12] The study was approved by the local ethics committee.

Imaging

All patients underwent mpMRI with triplanar T2-weighted, diffusion-weighted and dynamic contrast-enhanced sequences. In 68 patients (16%) mpMRI was performed elsewhere. In 347 patients (84%) MRI was performed without an endorectal coil on a whole body, 3 Tesla MAGNETOM® Skyra MRI system with 2 independent TimTX TrueShap transmit channels (Siemens, Iselin, New Jersey). The protocol and the sequence parameters were in accord with current international prostate MRI guidelines (supplementary table 1, http://jurology.com/).[13]

All images where analyzed by board certified radiologists who were not blinded to clinical information. A 5-point Likert scale obtained from the clinical radiology reports was used to designate ROIs as 1—highly unlikely, 2—unlikely, 3—equivocal, 4—likely and 5—highly likely to harbor clinically significant PCa. External mpMRIs without a Likert score were reviewed by the local radiologist. This Likert scale is a well established reporting scheme analogous to PI-RADS™ (Prostate Imaging Reporting and Data System) which has been used in several studies.[7,14,15]

Biopsy Protocol

Transperineal biopsies were performed by 3 urologists with several years of experience with standard TRUS guided biopsy. Prostates were biopsied according to the 20 Barzell zones. For optimal organ coverage needles were placed using the BiopSee® MRI/TRUS fusion biopsy system. In patients with suspicious ROIs, defined as a Likert score of 3 or greater on mpMRI, the lesions previously

Table 1

	Overall	Biopsy Naïve	Prior Biopsy	
			Neg	Pos
No. pts	415	163	86	166
Median age at biopsy (IQR)	64 (58—69)	63 (57—68)	64 (60—69)	65 (58—70)
Median ng/ml prostate specific antigen (IQR)	6.7 (4.4—9.6)	5.8 (4.4—8.9)	8.6 (5.7—13.0)	6.5 (4.1—8.6)
Median ml prostate vol (IQR)	46.0 (32.5—62.5)	44.6 (34.0—60.1)	53.6 (41.0—70.0)	41.4 (30.0—60.1)
Median days MRI-biopsy (IQR)	30 (14—60)	31 (18—55)	39 (20—81.0)	26 (9—54)
No. highest Likert score (%):				
No lesion or 1-2	124 (29.9)	49 (30.1)	36 (41.9)	39 (23.5)
3	76 (18.3)	36 (22.1)	18 (20.9)	22 (13.3)
4	126 (30.4)	52 (31.9)	18 (20.9)	56 (33.7)
5	89 (21.4)	26 (16.0)	14 (16.3)	49 (29.5)
No. Likert score 3 or greater ROIs (%):				
0	124 (29.9)	49 (30.1)	36 (41.9)	39 (23.5)
1	201 (48.4)	81 (49.7)	31 (36.0)	89 (53.6)
2	71 (17.1)	27 (16.6)	14 (16.3)	30 (18.1)
3-5	19 (4.6)	6 (3.7)	5 (5.8)	8 (4.8)
Median Likert score 3 or greater ROI max diameter (IQR)	11.0 (8.0—15.0)	11.0 (9.0—15.0)	10.0 (8.00—14.5)	12.0 (8.0—16.0)

identified by the T2-weighted sequence were superimposed on the real-time TRUS images. Nonrigid fusion was performed using the BiopSee MRI/TRUS fusion biopsy system.[16] Two to 4 additional cores were obtained after completing systematic biopsies from each ROI.

Histopathology

Each single core that was taken was evaluated separately by a uropathologist. Tumor length was measured in each needle core and reported as the MCCL in mm. PCa was defined as clinically significant in the presence of any Gleason 4 pattern (GS 7 or greater). However, in the absence of a clear consensus on clinical significance an additional 4 definitions were also applied to enable comparability with other studies. The definitions were 1) GS 3 + 4 or greater and MCCL 4 mm or greater, 2) GS 4 + 3 or greater, 3) GS 4 + 3 or greater, or MCCL 6 mm or greater and 4) GS 3 + 4 or greater, or MCCL 4 mm or

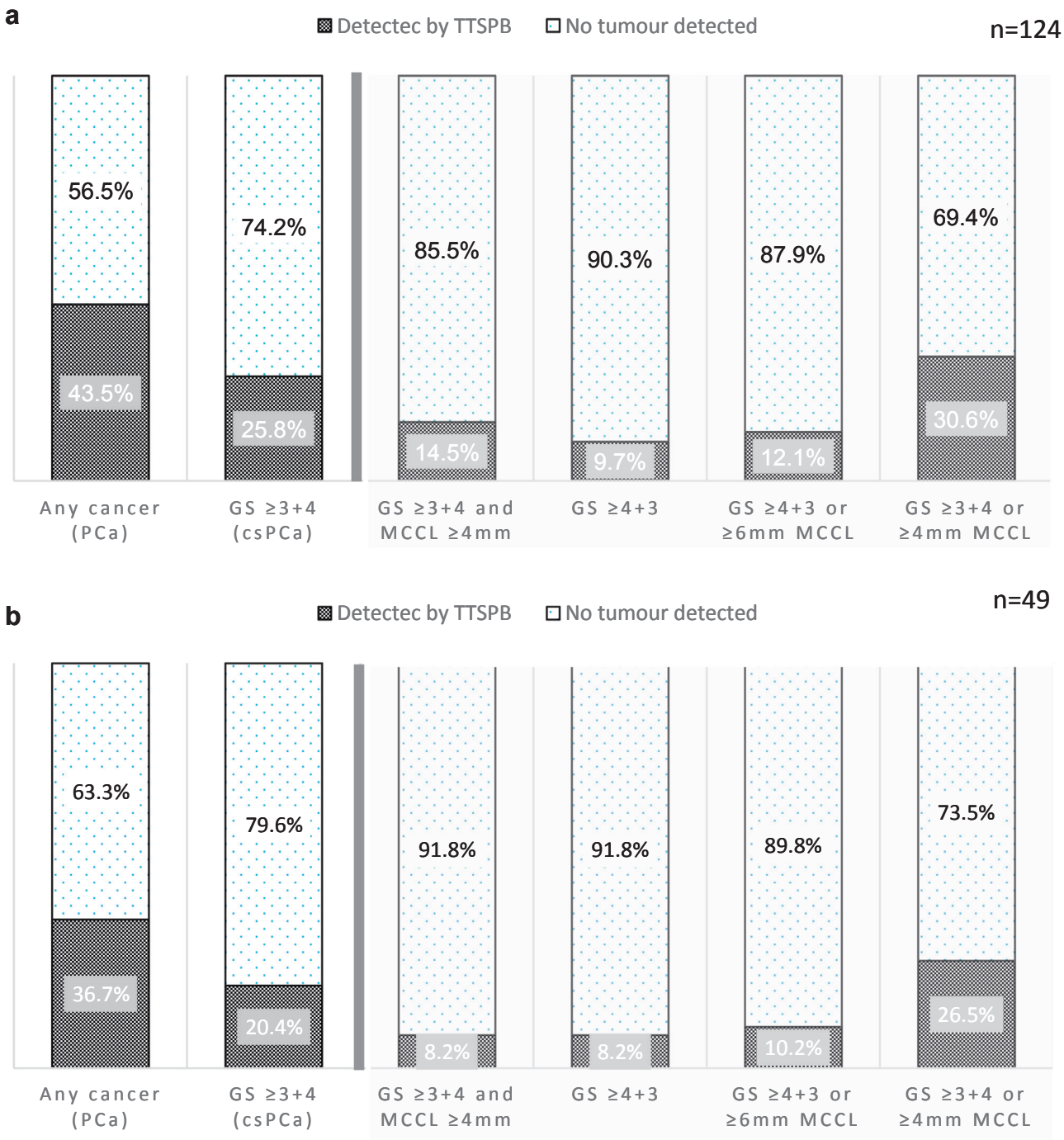

Figure 1. Diagnostic performance of transperineal template saturation prostate biopsy in patients in whom mpMRI revealed no ROI interest with Likert score of 3 or greater. Detection rate is displayed for different definitions of clinical significance, and in all 124 patients (*a*) and 49 biopsy naïve patients (*b*).

greater. The MCCL thresholds of 4 mm or greater and 6 mm were based on TTSPB studies defining the MCCLs that provided more than 95% sensitivity to detect lesions 0.2 ml or greater and 0.5 ml or greater, respectively.[7,17]

Data Analysis and Statistics

We compared the performance of TTSPB, FTB and the combination of TTSPB and FTB to detect PCa in patients with 1 or more ROIs and a Likert score of 3 or greater. The detection rate of csPCa is reported separately and for a combination of the 2 techniques. IBM® SPSS®, version 22.0 was used for descriptive statistics. The McNemar test was applied to compare the performance of different biopsy strategies. The unit of accuracy assessment was 1 patient (ie a whole prostate).

Diagnostic accuracy measures of sensitivity, specificity, overall accuracy, positive predictive value, negative predictive value and LRs along with the 95% CIs were calculated with MedCalc®, version 17.2. Interval LRs were calculated as previously described[18] to demonstrate changes in pretest probability resulting from mpMRI and FTB results. Tests were 2-sided and considered statistically significant at $p < 0.05$.

RESULTS

A total of 415 treatment naïve patients underwent mpMRI followed by TTSPB during the study period. Table 1 lists clinical and radiographic characteristics. GS was 6 and 7 in 90 (54.2%) and 76 patients (45.8%), respectively, who had a prior biopsy positive for PCa. A median of 40 TTSPB cores (range 30 to 55) and 3 FTB cores (range 2 to 4) were taken. [T1]

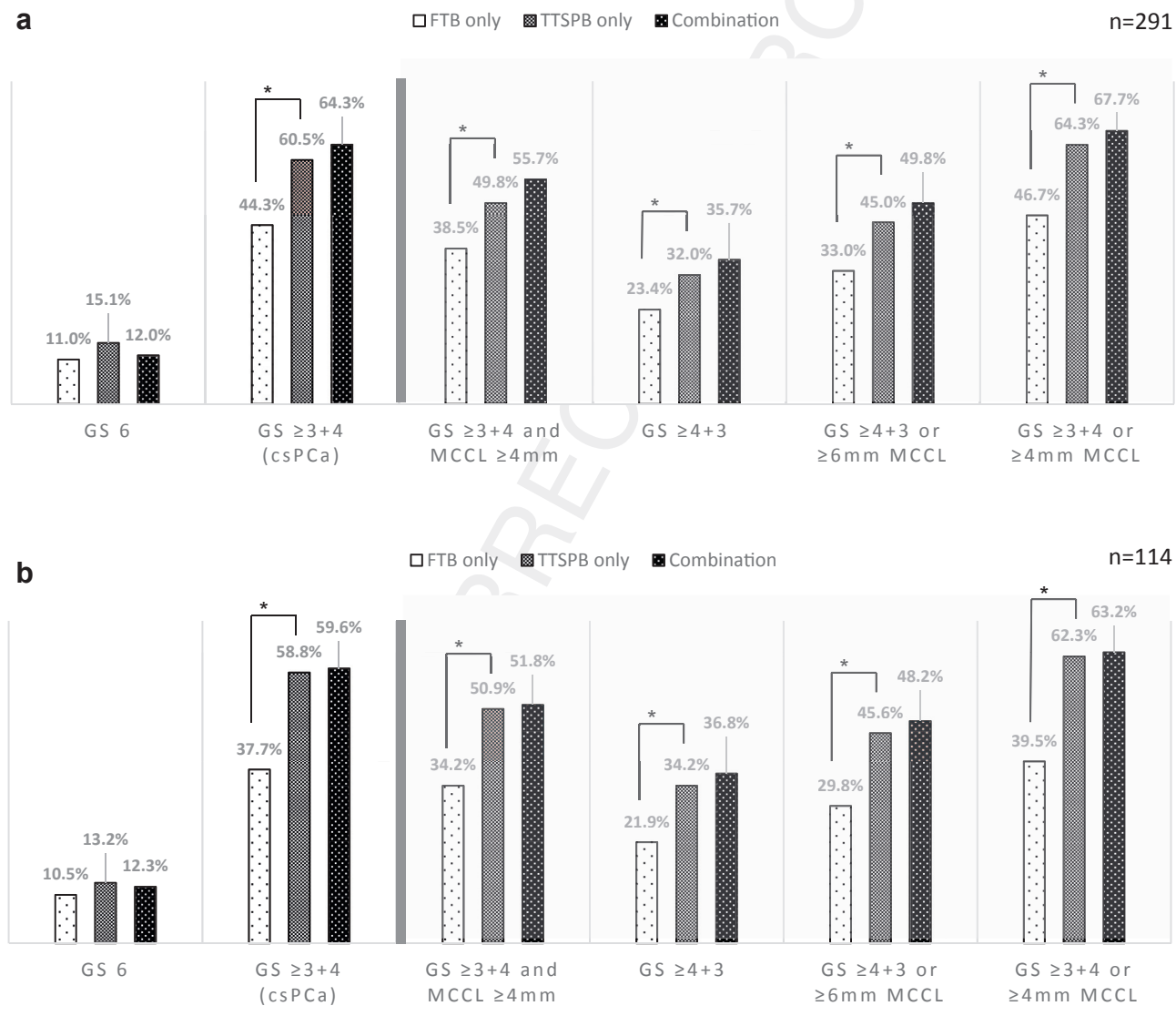

Figure 2. Detection rate of fusion guided targeted biopsy, transperineal template saturation prostate biopsy and combined approach in patients in whom mpMRI revealed at least 1 ROI with Likert score of 3 or greater. Detection rate is shown for different definitions of clinical significance and in all 291 patients (*a*) and 114 biopsy naïve patients (*b*). McNemar test was used to compare performance of FTB vs TTSPB to detect clinically significant prostate cancer. Asterisk represents $p < 0.05$.

On mpMRI unsuspicious ROIs, defined as a Likert score of less than 3, were found in 124 men (29.9%). Of these patients TTSPB detected any PCa [F1] in 54 (43.5%) and csPCa in 32 (25.8%) (fig. 1, *a*). When considering only biopsy naïve men, these rates were only slightly lower at 36.7% and 20.4%, respectively (fig. 1, *b*). Notably 4 patients (3.2%) had a GS 8 and 1 (0.8%) had GS 10 despite the absence of reported lesions on mpMRI.

In 291 patients (70.1%) at least 1 suspicious ROI (Likert score 3 or greater) was reported on mpMRI. TTSPB followed by FTB was successfully completed [F2] in all of these 291 patients. Figure 2 shows PCa the detection rates of combined biopsy, and FTB and TTSPB alone. The combined approach detected 222 PCa cases (76.3%), including 161 (55.3%) on FTB alone vs 220 (75.6%) on TTSPB alone ($p < 0.001$). CsPCa was detected by the combined approach in 187 cases (64.3%), including 129 (44.3%) on FTB alone vs 176 (60.5%) on TTSPB alone ($p < 0.001$).

Thus, adding FTB to TTSPB resulted in additional detection of 11 patients (3.8%) while performing FTB alone without TTSPB would have [F3] missed 58 (19.9%) who harbored csPCa. Figure 3 shows detection rates based on prior biopsy status and Likert scores.

To address a possible confounding effect of the FTB learning curve we compared the detection rate of csPCa in the first 146 cases with that in the last 145. The incidence of cases missed by the FTB approach decreased from 21.9% to 18.0% (supplementary figure, http://jurology.com/).

We performed an additional subgroup analysis of the detection of low and high risk PCa. GS 6 was diagnosed in 35 patients (12%) by the combined approach vs 32 (11%) by FTB and 44 (15%) by TTSPB alone ($p = 0.148$, table 2). High risk tumors [T2] (GS 8-10) were detected by the combined approach in 59 men (20.3%) and TTSPB alone again delivered performance superior to that of FTB alone (52 or 17.9% vs 36 or 12.4%, $p = 0.005$). When performing only FTB without TTSPB 3 patients (1%) with a GS 6 tumor and 23 (7.9%) with high risk PCa would have been missed.

Tumor detection on mpMRI is a crucial step in the diagnostic pathway of FTB. Therefore, we considered 54 and 32 of the 124 men with negative mpMRI but TTSPB detection of PCa and csPCa, respectively, in the accuracy analysis and they added to the FTB false-negative rate. For the specificity analysis cases diagnosed by FTB but not by TTSPB were classified as false-positive findings (supplementary table 2, http://jurology.com/). The sensitivity of mpMRI and FTB for csPCa was 84.6%

Table 2. *Gleason score differences (prognostic risk groups 1 to 5) detected by fusion targeted and transperineal template saturation prostate biopsies*

	No. TTSPB Results						
FTB Results	No Ca	GS 6	GS 3 + 4	GS 4 + 3	GS 8	GS 9-10	Total No.
No Ca	69	24*	21*	10*	3‡	3‡	130
GS:							
6	2†	9	17*	2*	0‡	2‡	32
3 + 4	0†	10†	35	9*	2‡	5‡	61
4 + 3	0†	1†	7†	16	4‡	4‡	32
8	0‡	0‡	1‡	2‡	12	5*	20
9-10	0‡	0‡	2‡	2‡	1†	11	16
Totals	71	44	83	41	22	30	291

* Upgraded TTSPB prognostic risk group in relation to FTB.
† Upgraded FTB prognostic risk group in relation to FTB.
‡ Upgraded to high risk category.

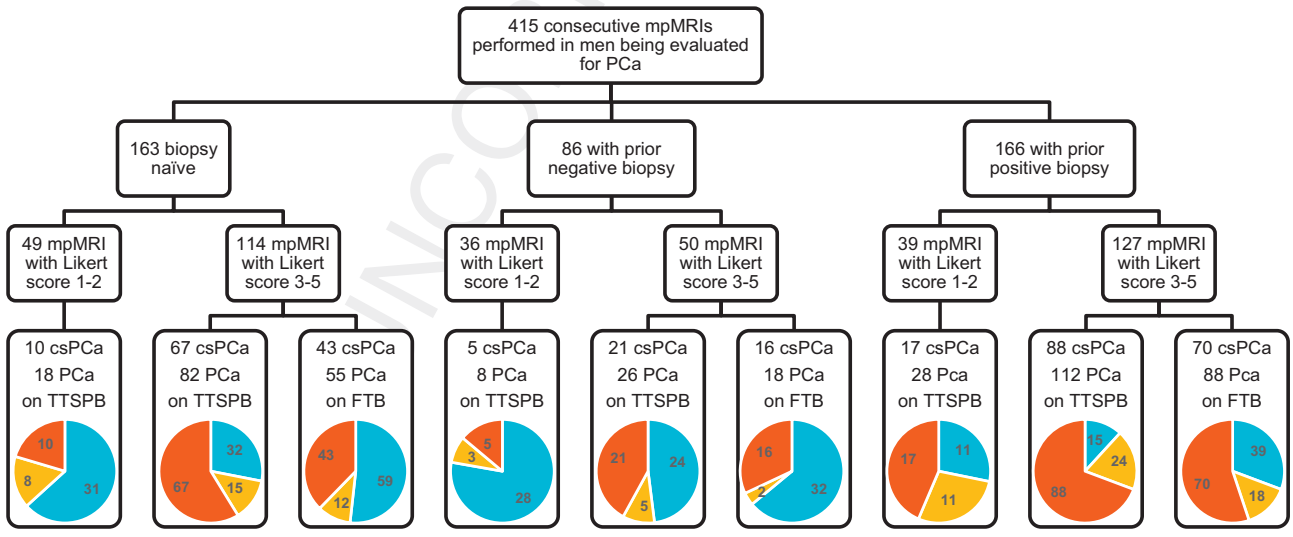

Figure 3. Detection rates of PCa and clinically significant PCa (Gleason score 7 or greater) based on prior biopsy status and mpMRI Likert score.

and 56.7% with a negative LR of 0.35 and 0.46, respectively. Table 3 shows details of the accuracy analysis. Supplementary table 3 (http://jurology.com/) lists LRs based on Likert scores.

The mean ± SD MCCL in patients with a suspicious ROI was 5.3 ± 4.1 and 6.0 ± 4.2 mm for PCa and csPCa, respectively. These means were significantly higher than in patients without a suspicious ROI on mpMRI, including 3.1 mm for PCa and 3.4 mm for csPCa ($p = 0.02$). Figure 4 shows the relationship between Likert scores and the presence of csPCa. TTSPB outperformed FTB for all Likert scores, including scores of 3, 4 and 5 ($p = 0.13$, <0.001 and 0.001, respectively).

There was a direct association between lesion size on mpMRI and csPCa detection, including 29% for ROI less than 5 mm, 33% for ROI 5 to 9 mm and 50% for ROI 10 mm or greater ($p = 0.019$, supplementary table 4, http://jurology.com/). External imaging revealed a comparable csPCa detection rate (supplementary table 5, http://jurology.com/).

DISCUSSION

Technological advances in mpMRI have led to the expectation that random biopsies of the prostate would no longer be necessary and could be replaced by targeted biopsies sometime in the near future, in accordance with the development of diagnostic pathways of other solid tumors.[1] In the current study we found that a significant number of men with negative mpMRI harbored clinically significant PCa. Furthermore, in the group with suspicious mpMRI 58 csPCa cases (19.9%) would have been missed without systematic biopsy (TTSPB). To our knowledge this is the first study evaluating the role of mpMRI and FTB based on highly extensive SB with a median number of 40 cores as the reference test.

Assessing the diagnostic error of mpMRI remains a major challenge. In previous investigations addressing mpMRI sensitivity and specificity for detecting PCa whole gland pathology (selection bias)[19–22] or standard TRUS guided biopsy (low accuracy) served as a reference standard.[23] This may explain the wide 44% to 87% range of reported sensitivity rates.[1]

Recently for the first time Ahmed et al assessed the accuracy of mpMRI compared to TTSPB as the reference test.[7] Although scans were reported by dedicated urological radiologists with special training, mpMRI missed 12% of patients with GS 7 or greater disease. In the current study radiologists with different years of experience with reading prostate MRI reviewed the imaging, which might be a reason for the lower sensitivity. However, the

Table 3. *Sensitivity, specificity, overall accuracy, positive and negative predictive values, and positive and negative likelihood ratios of detection of any prostate cancer and clinically significant prostate cancer (Gleason score 7 or greater) in all patients and in subgroups based on prior biopsy status*

	% Sensitivity (95% CI)	% Specificity (95% CI)	% Accuracy (95% CI)	% Predictive Value (95% CI)		Likelihood Ratio (95% CI)	
				Pos	Neg	Pos	Neg
Detection of any PCa							
Overall (415 pts):							
mpMRI	80.3 (75–85)	49.7 (41–58)	69.9 (65–74)	75.6 (72–79)	56.5 (49–63)	1.59 (1.3–1.9)	0.40 (0.3–0.5)
Fusion targeted biopsy	58.4 (52–64)	97.2 (93–99)	71.6 (67–76)	97.6 (94–99)	54.6 (51–58)	20.6 (7.8–54.4)	0.43 (0.4–0.5)
Biopsy naïve (163 pts):							
mpMRI	82.0 (73–89)	49.2 (36–62)	69.3 (62–76)	71.9 (66–77)	63.3 (51–74)	1.61 (1.2–2.1)	0.37 (0.2–0.6)
Fusion targeted biopsy	56.0 (46–66)	96.8 (89–100)	71.8 (64–79)	96.6 (88–99)	58.1 (53–63)	17.64 (4.5–69.8)	0.45 (0.4–0.6)
Neg prior biopsy (86 pts):							
mpMRI	76.5 (59–89)	53.9 (39–68)	62.8 (52–73)	52.0 (53–61)	77.8 (64–87)	1.66 (0.2–2.4)	0.44 (0.2–0.8)
Fusion targeted biopsy	52.9 (35–70)	100 (93–100)	81.4 (72–89)	100	76.5 (69–82)	—	0.47 (0.3–0.7)
Pos prior biopsy (166 pts):							
mpMRI	80.0 (72–86)	42.3 (23–63)	74.1 (67–81)	88.2 (84–91)	28.2 (18–41)	1.39 (1.0–2.0)	0.47 (0.3–0.8)
Fusion targeted biopsy	61.4 (53–70)	92.3 (75–99)	66.3 (59–73)	97.7 (92–99)	30.8 (26–36)	7.99 (2.1–30.4)	0.42 (0.3–0.5)
Detection of clinically significant PCa							
Overall (415 pts):							
mpMRI	84.6 (79–89)	44.4 (38–51)	64.6 (60–69)	60.5 (57–64)	74.2 (67–80)	1.52 (1.3–1.7)	0.35 (0.2–0.5)
Fusion targeted biopsy	56.7 (50–64)	94.7 (91–97)	75.7 (72–80)	91.5 (86–95)	68.5 (65–72)	10.68 (5.9–19.2)	0.46 (0.4–0.5)
Biopsy naïve (163 pts):							
mpMRI	87.0 (77–94)	45.4 (35–56)	65.0 (57–72)	58.8 (54–64)	79.6 (68–88)	1.59 (1.3–2.0)	0.29 (0.2–0.5)
Fusion targeted biopsy	54.6 (43–66)	98.8 (94–100)	77.9 (71–84)	97.7 (86–100)	70.8 (66–76)	46.9 (6.6–332.8)	0.46 (0.4–0.6)
Neg prior biopsy (86 pts):							
mpMRI	80.8 (61–93)	51.7 (38–65)	60.5 (49–71)	42.0 (34–50)	86.1 (73–93)	1.67 (1.2–2.3)	0.37 (0.2–0.9)
Fusion targeted biopsy	53.9 (33–73)	96.7 (88–100)	83.7 (74–91)	87.5 (63–97)	82.9 (76–88)	16.15 (4.0–66.1)	0.48 (0.3–0.7)
Pos prior biopsy (166 pts):							
mpMRI	83.8 (75–90)	36.1 (24–49)	66.3 (59–73)	63.3 (55–71)	56.4 (43–69)	1.31 (1.1–1.6)	0.45 (0.3–0.8)
Fusion targeted biopsy	59.1 (49–69)	86.9 (76–94)	69.3 (62–76)	88.6 (80–94)	55.2 (49–61)	4.5 (2.3–8.8)	0.47 (0.4–0.6)

Transperineal template saturation prostate biopsy was referent and since tumor detection on mpMRI is crucial step in fusion targeted biopsy diagnostic pathway, 32 men with false-negative mpMRI were included in fusion targeted biopsy accuracy analysis.

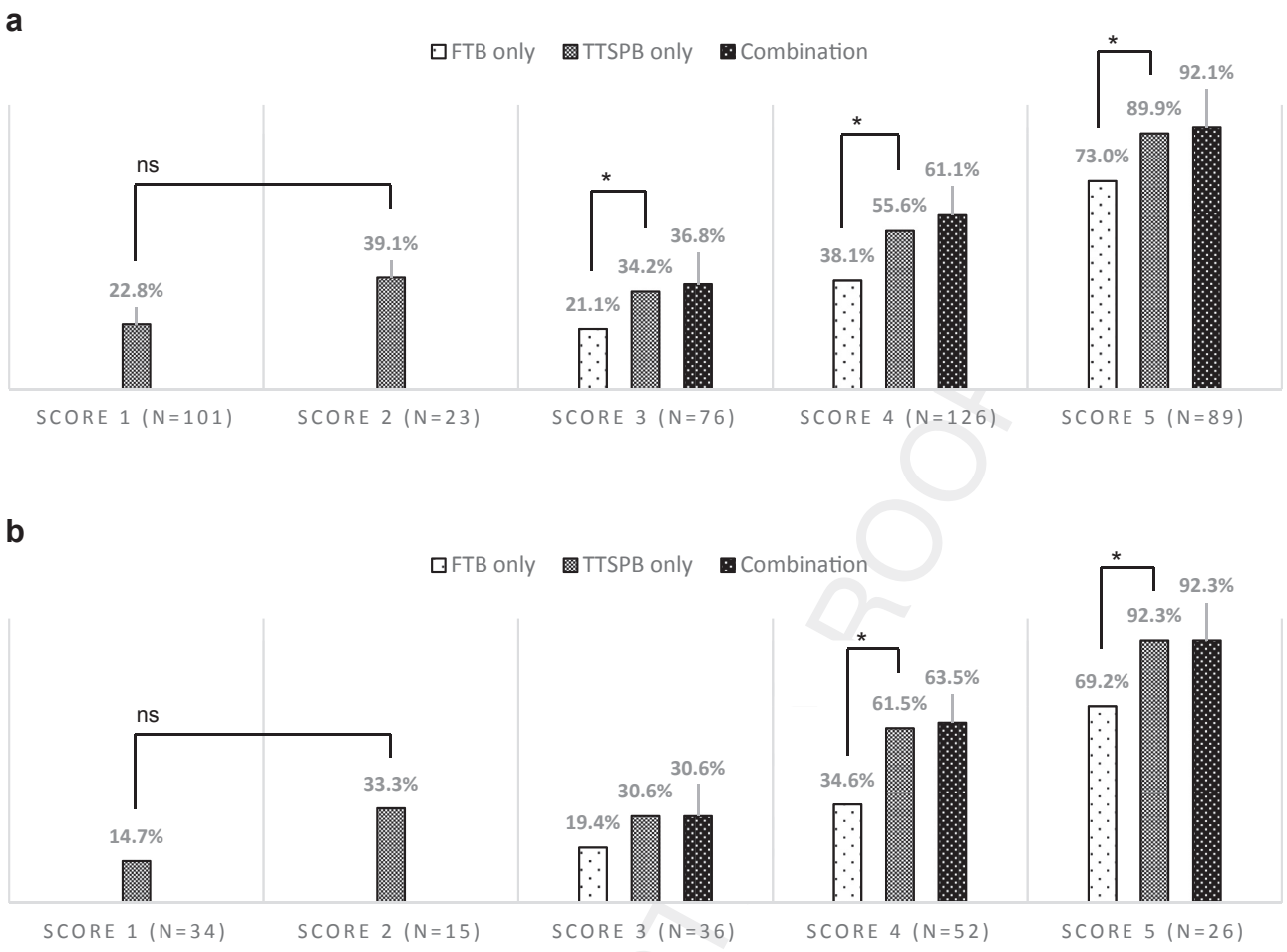

Figure 4. Diagnostic performance of fusion guided targeted biopsy, transperineal template saturation prostate biopsy and combined approach classified by highest Likert score on mpMRI. Detection rate is shown in all 415 patients (*a*) and 163 biopsy naïve patients (*b*). McNemar test was used to compare performance of FTB vs TTSPB to detect clinically significant prostate cancer. *ns*, nonsignificant. Asterisk indicates p <0.05.

detection of csPCa in 20.4% of biopsy naïve patients with negative mpMRI shows that MRI invisible cancer is common outside of prospective clinical trials. The false-negative rate remained significant at greater than 10% even when considering only tumors with a volume of 0.2 ml or greater and 0.5 ml or greater. The negative LR of unsuspicious mpMRI was 0.35 in the entire cohort, which is considered to indicate only a minor impact on the posttest probability.[24]

Evaluating the accuracy of FTB for detecting PCa faces the same challenges as mpMRI in regard to the reference test. Groups have investigated the accuracy of FTB by comparing it whole gland histology or standard TRUS guided biopsy.[3] Considering the known high false-negative rate of up to 50% for standard TRUS guided biopsy[7,8] the frequently detected superiority of FTB is not surprising.[3] However, a clear trend toward lower FTB accuracy was observed when a superior SB was performed.

Siddiqui et al found FTB to be superior to standard TRUS guided biopsy with 16% more cases of csPCa (GS 7 or greater) detected.[9] In a similar study Filson et al also found FTB to be superior to SB but they detected only 13% more GS 7 or greater tumors by replacing standard TRUS guided biopsy with Artemis™ guided mapping biopsy.[25] Since FTB alone would have missed 60 cases of csPCa, the investigators concluded that the most accurate results were achieved by combining FTB and software guided SB.

Radtke[26] and Hansen[27] et al compared FTB to software guided TTSPB with a median of 24 cores. While the first study showed no advantage of any approach for detecting csPCa, the latter investigation revealed the superiority of TTSPB with an overall 9% higher detection rate (p <0.001). We could further confirm this trend. With a median of 40 cores our software guided TTSPB detected 19.9% more csPCa cases than FTB alone in an unselected

and consecutive group of men being evaluated for PCa. With a negative LR of 0.6, FTB could not sufficiently lower the posttest probability to rule out PCa.[24]

One could argue that this poorer performance was due to poor execution of the FTB technique. Recently reported detection rates of csPCa based on software based fusion were 16%, 33% and 69% in the study by Filson et al,[25] and 13%, 35% and 74% in the study by Mariotti et al[28] for scores of 3, 4 and 5, respectively, for lesions detected by mpMRI. With a slightly higher detection rate of 21%, 38% and 73%, respectively, the performance of FTB in the current study is comparable to that in the other reports, validating our FTB technique. Therefore, we do not attribute the better performance by TTSPB than by FTB to low accuracy of our FTB technique but rather to the significantly higher detection rate of software guided TTSPB compared to other SB techniques reported to date.

Yet FTB remains an error prone process. Radtke et al evaluated the diagnostic yield of mpMRI and FTB using whole gland histology.[19] They found that FTB performed less accurately to detect csPCa since it missed lesions that were accurately detected by mpMRI. A similar trend was observed in the current study with significantly higher sensitivity of mpMRI compared with FTB (csPCa detection 84.6% vs 56.7%).

It was believed that the inaccuracy of the FTB method[29] could be overcome by an in bore MRI guided biopsy technique using a real-time image of the patient prostate. However, a systematic review did not show a higher detection rate for csPCa than for FTB despite the greater technical effort and higher costs.[30] Therefore, we believe that at the moment no targeted biopsy method can reliably and constantly place the needle in the ROI defined by imaging and achieve the higher accuracy of mpMRI in the detection of csPCa.

Limitations of this investigation are its retrospective nature and the heterogeneous population of men, including patients undergoing initial or repeat biopsy, patients on active surveillance or patients being evaluated for focal therapy. However, a subgroup analysis of biopsy naïve patients revealed a similar detection rate. Furthermore, multiple radiologists not blinded to clinical data with different years of experience with reading prostate mpMRIs reported the examinations using a Likert score instead of the more common PI-RADS score. In contrast, either could also be considered a strength of the study since it more realistically reflects real-world clinical circumstances. Finally, we cannot rule out that cancers missed by TTSPB and prostate swelling during fusion compromised the FTB detection rate.

CONCLUSIONS

Based on our analysis mpMRI alone should not be performed as a triage test in men being evaluated for suspected PCa due to a substantial number of false-negative csPCa results. SB using TTSPB outperformed software based FTB. Therefore, it will remain crucial in the diagnostic pathway of PCa until new modalities can provide reliable accuracy in daily clinical practice.

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EDITORIAL COMMENTS

In this clinically relevant study the authors assessed the diagnostic accuracy of mpMRI and FTB compared to TTSPB in a cohort of 415 consecutive patients.

Beyond the study limitations which are clearly acknowledged by the authors, such as its retrospective nature and heterogenous population, the current study highlights the limitations of mpMRI with 25.8% of negative mpMRI cases harboring csPCA. Indeed, 19.9% of csPCa cases would have been missed if FTB alone has been performed, leading the authors to question the reliability of the FTB alone approach.

Of patients with suspicious mpMRI (Likert score 3 to 5) FTB detected csPCa in 44.3%, TTSPB detected csPCa in 60.5% and the combined approach detected csPCa in 64.3%. TTSPB outperformed FTB alone while the combined strategy appeared to be best, as supported by other contemporary studies (reference 27 in article). Combined FTB and TTSPB biopsies provided more complete and reliable sampling (reference 26 in article).

Currently mpMRI is limited in the detection of Gleason pattern 3 and possibly also in the detection of cribriform pattern 4.[1] This is of the upmost importance in the context of active surveillance and focal therapy strategies that cannot rely on sampling an index lesion, potentially missing contralateral, multifocal and even clinically significant disease.

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Mortezavi et al provide an important contribution in this study evaluating the accuracy of mpMRI and FTB compared to a TTSPB reference standard. All 415 men underwent mpMRI and TTSPB. The 291 men (70%) with abnormal MRI also underwent FTB. This study nicely complements PROMIS (Prostate MRI Imaging Study) by evaluating MRI and FTB instead of conventional TRUS biopsy (reference 7 in article).

The study has 3 particularly notable findings. 1) Of the men with a normal mpMRI 26% had csPCa. This exceeds the 11% reported in PROMIS (reference 7 in article). To our knowledge it is unknown which study more accurately reflects real-world MRI performance. 2) FTB alone would have missed csPCa in 58 men (20%) with an abnormal MRI. TTSPB over diagnosed 12 men with Gleason 6 cancer but found an additional 16 men with Gleason 8-10. 3) A strategy in which only men with an abnormal MRI underwent biopsy (FTB without systematic sampling) would have missed csPCa in 90 men (22%). This is a strong argument that this approach may be ill advised despite its attractiveness in principle.

Instead, we suggest considering clinical information along with MRI to improve decision making about biopsy[1] and combining FTB with systematic biopsy to maximize csPCa detection (reference 25 in article).

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